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Letter to the Editor

## Optimum wavelength characteristics for phototherapy utilizing deep ultraviolet light-emitting diodes

In the early 1980s, 313-nm wavelength was reported to have potential efficacy for treating psoriasis [1,2]. A fluorescent lamp emitting selective ultraviolet B (UVB) light ranging from 311 to 313 nm was developed for narrowband UVB therapy and widely used to treat various skin diseases, such as psoriasis, vitiligo, atopic dermatitis, and mycosis fungoides [3–5]. Narrowband UVB lamps contain mercury, however, and thus have a large environmental burden. In the early 2000s, targeted phototherapy devices using a xenon-chloride excimer laser or lamp emitting 308 nm as a mercury-free light source were developed to treat localized lesions without unnecessary exposure of the unaffected skin to UV light [6], but these devices are costly and therefore not suitable for treating large areas. The luminous efficiency of deep UV light-emitting diodes (DUV-LEDs) has remarkably improved [7]. DUV-LEDs are also a mercury-free light source, and can be used for large area devices by configuring multiple DUV-LEDs. Various device types with reduced size and weight can be designed using DUV-LEDs. Furthermore, DUV-LEDs with an optimum peak light wavelength can be used for phototherapy because DUV-LEDs are made of AlGaN, and the emission wavelength can be changed by altering the composition ratio of Al and Ga [8]. The full width at half maximum (FWHM; the wavelength width at 50% of the maximum intensity) of DUV-LEDs differs from that of traditional light sources such as the narrowband UVB and excimer lamps. The FWHM of a narrowband UVB lamp or excimer light source is approximately 5 nm [9], while the FWHM of the DUV-LEDs available for commercial use is approximately 10 to 20 nm. Even if it has the same peak wavelength, as FWHM increases, light on the short wavelength side relatively increases. Because the absorption coefficient of DNA greatly changes at wavelengths around 300 nm [10], slight differences in the spectral distribution may largely affect the clinical results. Therefore, we studied the optimum wavelength characteristics when utilizing DUV-LEDs for phototherapy.

Jurkat cells were used to investigate apoptosis and DNA damage as an in vitro model of T cell-mediated disease. Apoptosis is considered a measure of phototherapy efficacy. DNA damage, and the formation of cyclobutane pyrimidine dimers (CPDs) and (6-4) photoproduct (6-4PP) were measured as deleterious effects of phototherapy. The cells were irradiated with UVB light ranging from 280 nm to 320 nm in 5-nm steps and incubated for 24 h after irradiation in 5% CO2 at 37 °C in a humidified incubator. After incubation, apoptosis was measured. The slope of the dose-apoptosis curves decreased as the wavelength increased (Fig. 1a), and sharply decreased as the wavelength exceeded 295 nm. The dose required for 50% of the cells to undergo apoptosis (50% apoptosis dose) was 6 mJ/cm$^2$ (280 nm), 5 mJ/cm$^2$ (285 nm), 7 mJ/cm$^2$ (290 nm), 10 mJ/cm$^2$ (295 nm), 32 mJ/cm$^2$ (300 nm), 84 mJ/cm$^2$ (305 nm), 326 mJ/cm$^2$ (310 nm), 752 mJ/cm$^2$ (315 nm), and 1232 mJ/cm$^2$ (320 nm; Fig. 1b). The formation of CPD and 6-4PP was also measured. CPD formation was lowest at 290 nm in the range from 280 nm to 300 nm, and at 315 nm in the range from 300 nm to 320 nm (Fig. 1c). The formation of 6-4PP decreased with a decrease in the wavelength and was lowest at 315 nm (Fig. 1d). We considered the wavelength range above 300 nm because of the high erythemal action coefficient below 300 nm, making it unsuitable for clinical use. In addition, dose-CPD curves were measured using an enzyme-linked immunosorbent assay kit. The slope of the dose-CPD curve decreased with an increase in the wavelength (Fig. 1e). The slopes of the dose-CPD curves and the dose-apoptosis curves sharply decreased at wavelengths above 295 nm.

The formation of CPD and 6-4PP following irradiation with the 50% apoptosis dose was lowest at 315 nm. We hypothesized that the optimum wavelength for DUV-LED phototherapy – that is, a relatively high rate of apoptosis and relatively low CPD production – would be around 315 nm. For verification, we calculated the action coefficient of apoptosis and CPD from the dose-apoptosis curves (Fig. 1a) and the dose-CPD curves (Fig. 1e). We defined the slope in the linear region as the action coefficient and normalized it by each maximum value (Fig. 1f). We also evaluated the relative action coefficient at each wavelength calculated by the following formula: Relative action coefficient (λ) = Apoptosis action coefficient (λ) / CPD action coefficient (λ), where λ = 300, 305, 310, 315, or 320 nm. The relative action coefficient was 0.8 (300 nm), 0.7 (305 nm), 0.7 (310 nm), 1.3 (315 nm), and 1.6 (320 nm), respectively (Fig. 2). The wavelength at which the apoptosis action coefficient exceeded the CPD action coefficient was 285 nm to 297 nm and longer than 312 nm (Fig. 1f). The wavelength range from 285 nm to 297 nm is not suitable for clinical use because it has a high erythemal action coefficient. On the other hand, the longer the wavelength, the longer the irradiation time needed for treatment. Therefore, we concluded that the optimum peak wavelength when utilizing DUV-LEDs with an approximately 15-nm FWHM for ultraviolet phototherapy is 312 nm.

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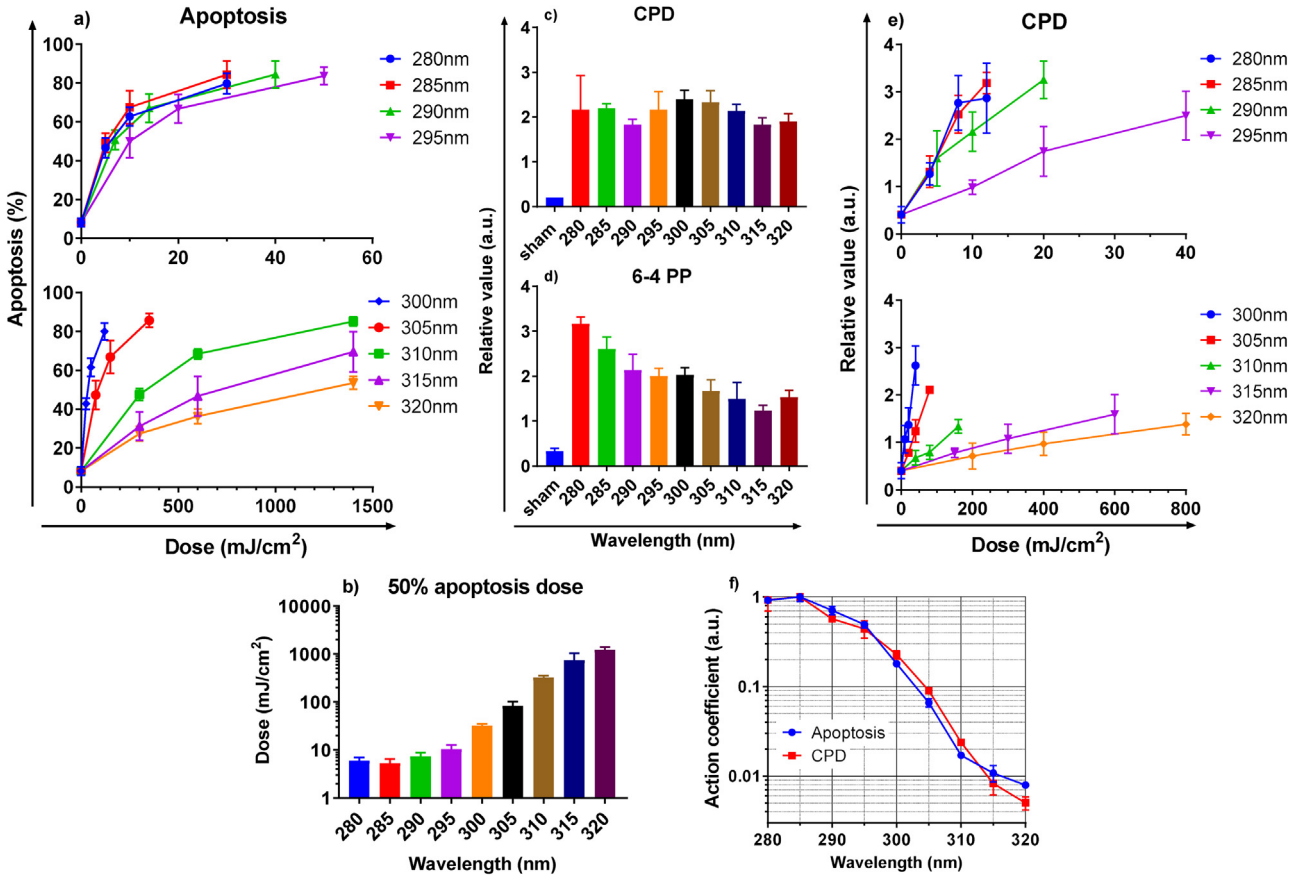


**Fig. 1.** a) Irradiation dose-apoptosis curves. b) The 50% apoptosis dose obtained from the irradiation dose-apoptosis curves at each wavelength. Cells were irradiated with UVB light from 280 nm to 320 nm in 5-nm steps and incubated for 24 h after irradiation in 5% $CO_2$ at 37 °C in a humidified incubator. Values are expressed as the mean ± standard deviation (SD) (n = 3/wavelength). c) CPD, d) 6-4PP production after irradiation with the 50% apoptosis dose at each wavelength. Cells were irradiated with the 50% apoptosis dose at each wavelength. DNA was isolated immediately after irradiation and CPD and 6-4PP formation was measured using enzyme-linked immunosorbent assay kits. Values are expressed as the mean ± SD (n = 3/wavelength). e) dose-CPD curves. Cells were irradiated with UVB light from 280 nm to 320 nm in 5-nm steps. The DNA was isolated immediately after irradiation and CPD formation was measured using an enzyme-linked immunosorbent assay kit. Values are expressed as the mean ± SD (n = 3/wavelength). f) Action coefficient spectrum of apoptosis and CPD calculated from Fig. 1a and e. Values are normalized by each maximum value and expressed as the mean ± SD (n = 3/wavelength).

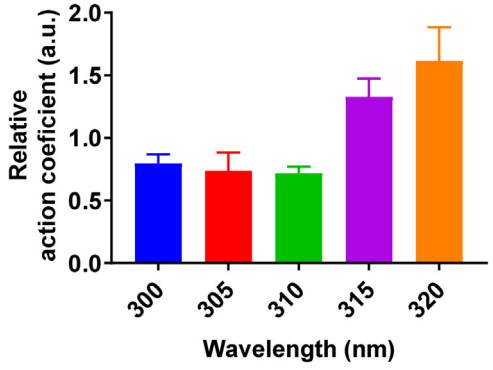


**Fig. 2.** Relative action coefficient at each wavelength calculated as the ratio of the apoptosis action coefficient and the CPD action coefficient. Values are expressed as the mean ± SD (n = 3/wavelength).

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## Conflict of interests

The authors declare no conflicts of interest.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jdermsci.2019.01.006.

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